Kidney International, Vol. 57 (2000), pp. 341–342

EDITORIAL

Hormone replacement therapy in postmenopausal women with end-stage renal disease[1]

Since the life expectancy of women has increased substantially over the past several decades, women are living a larger portion of their lives following menopause and in a state of estrogen deficiency. Following menopause, the risk of coronary artery disease increases substantially and estrogen deficiency contributes to the development of osteoporosis and hip fractures in older women [1, 2]. Hormone replacement therapy with estrogen compounds has been shown to alleviate the symptoms of menopause, decrease the incidence of coronary artery disease and hip fractures, improve the lipid profile, retard or prevent the development of osteoporosis, and possibly preserve cognitive function and prevent the development of dementia [1–5]. The adverse effects of hormone replacement therapy include an increased incidence of endometrial hyperplasia that can be nearly eliminated by the administration of progesterone in addition to estrogen [1]. While the increased risk of endometrial hyperplasia and endometrial cancer in postmenopausal women receiving hormone replacement therapy is established, it remains unclear if postmenopausal women receiving hormone replacement therapy have a higher risk of breast cancer, and the risk of this side effect of hormone replacement therapy remains controversial [5, 6]. Hormone replacement therapy is also associated with a higher incidence of thromboembolism [7].

Patients with end-stage renal disease (ESRD) are at risk for the development of renal osteodystrophy and they have a higher risk for accelerated atherosclerosis and cardiovascular disease compared to people in the general population [8, 9]. Thus, the adverse effects of estrogen deficiency may be particularly evident in women with ESRD and women with ESRD may potentially benefit from hormone replacement therapy. Conversely, women with ESRD may also have a higher incidence of adverse effects of hormone replacement therapy, including an increased incidence of cancer due to possible abnormalities in immune surveillance from chronic uremia and/or women with ESRD receiving hormone replacement therapy may have a higher risk of thrombosis of vascular access.

Use of hormone replacement therapy in the general population of postmenopausal women varies considerably based on the demographics of the study population, but some population-based studies demonstrate that about one fourth to one third of postmenopausal women receive hormone replacement therapy [10, 11]. Recent studies using USRDS data have demonstrated that approximately 10% of women with ESRD are treated with hormone replacement therapy [12]. Stehman-Breen, Gillen, and Gipson also document that about 10% of women with ESRD receive hormone replacement therapy, and they report for the first time the clinical characteristics associated with use of hormone replacement therapy in women with ESRD [11]. Using USRDS data, Stehman-Breen, Gillen, and Gipson found that postmenopausal women with ESRD were more likely to be white, ambulatory, have a college education, and were more likely to be younger. In addition, women with ESRD receiving hormone replacement therapy were more likely to be maintained by peritoneal dialysis and to not be diabetic.

It is remarkable that the use of hormone replacement therapy in women with ESRD who are at higher risk for cardiovascular disease, bone disease, and cognitive impairment is only 10%. Thus, women with ESRD who might substantially benefit from hormone replacement therapy are significantly undertreated compared to the general population. Given the substantial protection from cardiovascular disease that hormone replacement therapy provides in postmenopausal women, physicians caring for such women should ask why women with ESRD are significantly undertreated compared to the general population? Is it because they are perceived as unlikely to benefit from such therapy due to chronic illness and a potentially shortened life expectancy? Is it because women with ESRD might have a higher risk of endometrial hyperplasia and the potential risk of breast cancer compared to the general population, or is it because such therapy may increase the risk of thromboembolism and clotting of vascular access? The answers to these and other questions are unknown, but such information will be important to obtain so that physicians caring for women with ESRD and women with ESRD understand the benefits and risks of hormone replacement therapy.

[1] This editorial was submitted to accompany the article by Stehman-Breen, Gillen, and Gipson [11]. The Editors regret the omission.

Key words: estrogen, coronary artery disease, ESRD, osteoporosis, atherosclerosis.

Stehman-Breen, Gillen, and Gipson found that women with ESRD who were ambulatory were twice as likely and women with a college education were three times as likely to receive hormone replacement therapy, while women who were black and older were less likely to receive hormone replacement therapy. These results are not dissimilar from the demographics of hormone replacement therapy in the general population [12]. These findings suggest that similar medical and socioeconomic influences are involved in the decision to use hormone replacement therapy in women with ESRD as compared to the general population. However, as pointed out above, the decision to recommend hormone replacement therapy by the physician or the decision to take hormone replacement therapy by women with ESRD is much less than the general population. The reasons for this substantially lower use of hormone replacement therapy in women with ESRD need further study.

While it is tempting and not unreasonable to apply recommendations for the general population to women with ESRD, it is important to note that women with ESRD are likely to have specific considerations for hormone replacement therapy. For example, renal failure has been shown to alter estrogen metabolism and the biological beneficial and adverse effects of estrogen with or without progesterone therapy might be different in women with ESRD compared to the general population [13, 14]. Such alterations in estrogen metabolism might influence the cardioprotective benefits of estrogen therapy or could have adverse effects related to a higher incidence of thromboembolism and access thrombosis in women with ESRD. In addition, the timing of initiation of therapy is likely to be important. Women with ESRD may develop estrogen deficiency and the complications of estrogen deficiency at an earlier age compared to the general population. While hormone replacement therapy is cardioprotective in women without a history of cardiac disease, it is unclear if there is a beneficial effect in women with established cardiac disease [6, 15]. Thus, if initiated after the development of cardiovascular disease, the benefits of hormone replacement therapy in women with ESRD may not be realized.

Before an evidence-based approach to hormone replacement therapy in women with ESRD can be formulated, new data need to be acquired. A number of observational studies and clinical trials are needed, including determining the average age of menopause in women with ESRD, the association of menopause with cardiovascular risk factors in women with ESRD, the effects of hormone replacement therapy on serum lipids in women with ESRD, and the effects of hormone replacement therapy on cardiovascular outcomes in women with ESRD [13]. Additional studies such as the one by Stehman-Breen, Gillen, and Gipson [11] are to be encouraged, so that women with ESRD can make an educated decision about hormone replacement therapy.

Sharon P. Andreoli
Departments of Pediatrics and the Herman B. Wells Center for Pediatric Research, Indiana University School of Medicine, Indianapolis, Indiana, USA

Correspondence to Sharon P. Andreoli, M.D., James Whitcomb Riley Hospital for Children, Wells Research Center 2626, 702 Barnhill Drive, Indianapolis, Indiana 46202, USA.

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